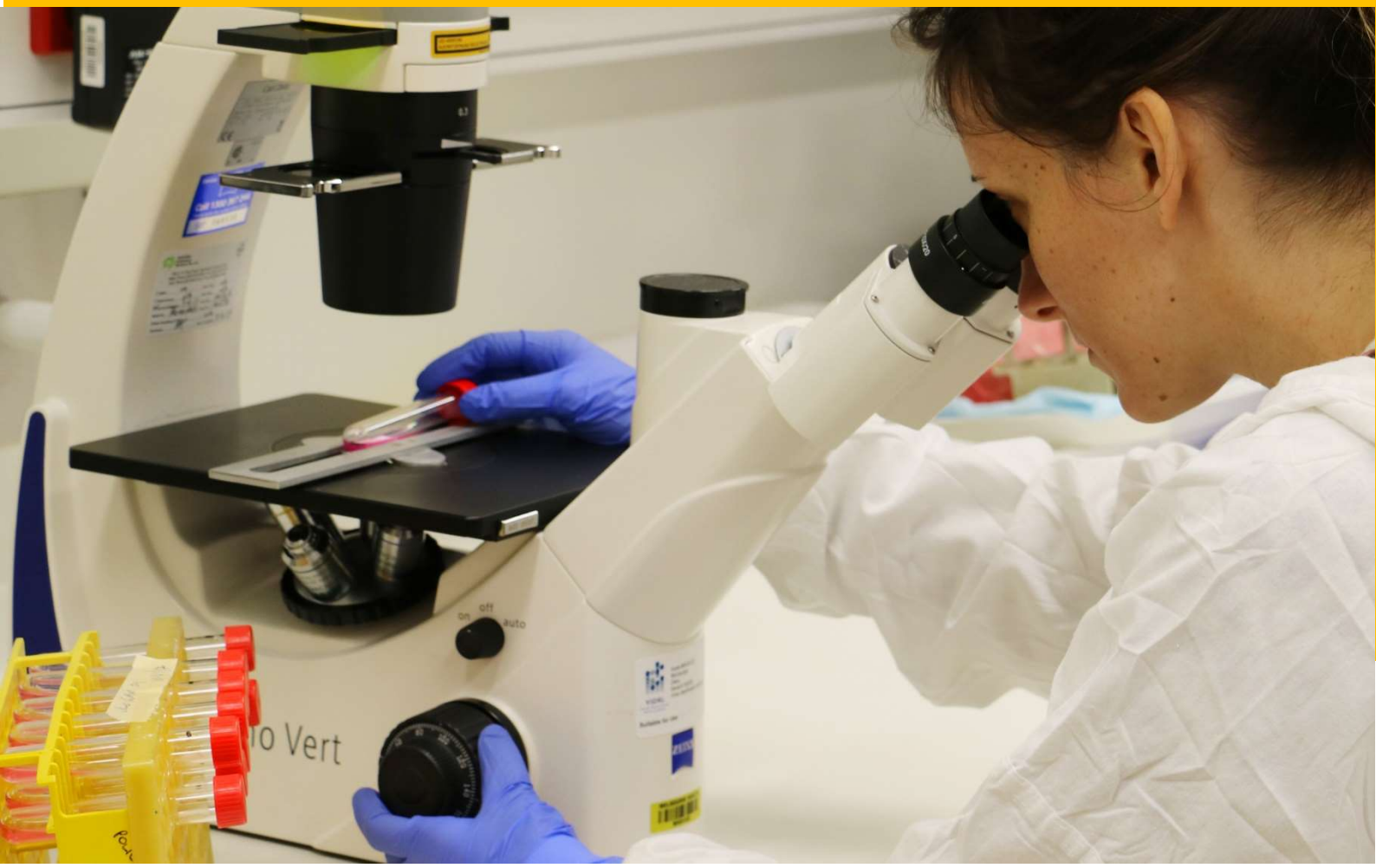
Measles and Rubella Molecular Epidemiology: Australia 2019



Victorian Infectious Diseases Reference Laboratory

Summary Report

VIDRL
Victorian Infectious Diseases Reference Laboratory

Doherty Institute
A joint venture between the University of Melbourne and the Royal Melbourne Hospital

1. Background

The measles and rubella laboratory at the Victorian Infectious Diseases Reference Laboratory (VIDRL) serves as the National Reference Laboratory for Australia and a WHO Regional Reference Laboratory for the Western Pacific Region. This laboratory provides a reference service for the detection and molecular genotyping of measles and rubella virus strains as part of its National Reference Laboratory function. Important aspects of laboratory molecular surveillance of measles and rubella at VIDRL during the post elimination phase include (i) genetic characterisation of circulating wild-type viruses to determine transmission events/pathways and support molecular epidemiological studies; (ii) differentiating vaccine strains from wild-type virus during outbreaks and (iii) monitoring the absence or persistence of endemic measles and rubella transmission.

Following a retrospective molecular epidemiological survey of Victorian measles strains from 1973-1998 (at the time the world's largest), VIDRL's measles molecular surveillance from 1999 indicates that measles transmission has been interrupted within Australia. Measles molecular epidemiological surveillance is widely accepted as a key criterion demonstrating the absence of an endemic genotype, and helping to demonstrate that a high proportion of cases and outbreaks are import-related. VIDRL's work has improved understanding of the global distribution of measles genotypes by defining those from source countries that were imported into Australia, and has identified three previously undescribed measles genotypes. Optimal periods for measles virus RNA recovery from specimens have been defined, together with validation of nucleic acid based measles detection direct on patient samples specifically for the measles vaccine strain and/or subsequent genotyping. The addition of an assay targeting a hypervariable region of the measles genome to complement standard genotyping methods will improve the genetic resolution when the genetic diversity of circulating measles strains diminishes.

More recently, genotyping evidence played an important role in verifying the interruption of endemic rubella virus in Australia for the years 2012 to 2017, one of the few countries in the region to have achieved this milestone. Australia was also successful in maintaining its

measles elimination status for 2018 with genotyping evidence continuing to support the absence of endemic measles transmission.

This annual report provides a comprehensive description on the molecular epidemiology of measles and rubella in Australia for year 2019 and provides virological evidence supporting the sustained interruption of endemic transmission, of both measles and rubella viruses, in 2019.

2. Measles Molecular Epidemiology Australia, 1 January to 31 December 2019

The number of samples tested for measles RNA by real-time PCR during the reporting period was 1606, an increase of 101% over the previous year. Of these, 296 (18.5%) samples had measles virus RNA detected from 231 cases.

A measles genotype was obtained from 210 cases of which 172 (74.5%) were wild-type strains and 38 (16.5%) vaccine strains (Table 1). The remaining 21 cases (9%) had an RNA copy number that was too low for genotyping (untypable).

From a minority of jurisdictions with local measles genotyping capabilities, fourteen N450 sequences were submitted to VIDRL or to the Measles Nucleotide Surveillance (MeaNS) database for inclusion in the national database and are included in this report.

Wild-type measles cases were detected in 45 of the 52 reporting weeks (Figure 1) with circulation detected in all Australian States and Territories (Figure 2). At least 59 known importation events from 23 countries or regions were identified as possible sources (Figure 3-4 or Table 2). Only 2 wild-type measles genotypes, B3 and D8, were identified during this period. In Australia, the genotype lineages identified reflects the source of imported virus, which is consistent with a genotypic pattern seen in countries that have eliminated measles.

Genotype D8, the most common type detected (n=135), circulated following at least 32 separate importation events from foreign countries. This genotype was predominately introduced into Australia from New Zealand, Thailand and Vietnam. Other source countries/regions included Bangladesh, Chile, India, Indonesia, Lebanon, Malaysia, Singapore, Myanmar and South East Asia (Figure 3). The genetic lineage for the majority of measles genotype D8 cases identified in Australia could be matched to a WHO named strain or to a

genetic viral strain found circulating in other parts of the world. The nucleotide sequence for the latter was often consistent with the source country of importation (Figure 5). Dagon Seikkan, Osaka, Samut Sakhon, Thiruvananthapuram and Gir Somnath were all named strains identified in 2019 (Figure 5, Table 2). For the very small number of cases with no exact N450 sequence match in MeaNS, epidemiologic data indicated a known imported primary case.

Based on phylogenetic analysis, the weekly distribution of measles genotype D8 grouped by phylogenetic clustering (Figure 3) clearly shows the interruption all genetic clusters except for one, Cluster 1 (Figure 3). However, supporting epidemiologic evidence indicates that this Gir Somnath lineage was the result of many re-incursions throughout the year rather than one continuous transmission chain. Thus phylogenetic analysis coupled with strong epidemiological data has provided strong evidence that Australia has sustained the interruption of endemic measles transmission of this genotype in 2019.

There were 51 cases of measles genotype B3, with epidemiologic and genetic data consistent with imported or imported-related virus (Figure 4, Table 2). Introduction of this genotype originated from New Zealand, Pakistan, Samoa, Thailand and the United Arab Emirates. However, most introductions into Australia were from the Philippines where this genotype remains endemic (Figure 4). Some measles B3 cases in Australia were linked to the Gombak named strain, Kabul named strain or the Marikina named strain while others had exact N450 sequence match to other geographical strains found in MeaNS (Figure 6). Of note is a large cluster of genotype B3 cases in the final quarter of 2019 (Figure 4, cluster 9) and the start of 2020 (data not provided). These cases caused outbreaks across Australia and were due to imported virus primarily from Samoa, albeit the virus source originated from New Zealand. Cases of this lineage, detected in the 2nd and 3rd quarter in return travellers from New Zealand is consistent with this finding.

As with genotype D8 identified in Australia, the weekly distribution of measles genotype B3 grouped by phylogenetic clustering provides solid evidence that Australia has sustained the interruption of endemic measles B3 transmission in 2019.

Table 1 and Table 2 provides a de-identified line-listing of measles vaccine cases and wild-type measles genotyping data by state and territory, virus lineage and WH0 representative strain, respectively.

3. Rubella Molecular Epidemiology Australia, 1 January to 31 December 2019

The prevalence of rubella virus infection in Australia remains extremely low. In 2019, 215 specimens were referred to VIDRL for rubella nucleic acid testing of which there were no RNA detections by the rubella real-time PCR.

Figure 1: Distribution of wild-type measles genotype identified at VIDRL epi-week, January to December 2019.

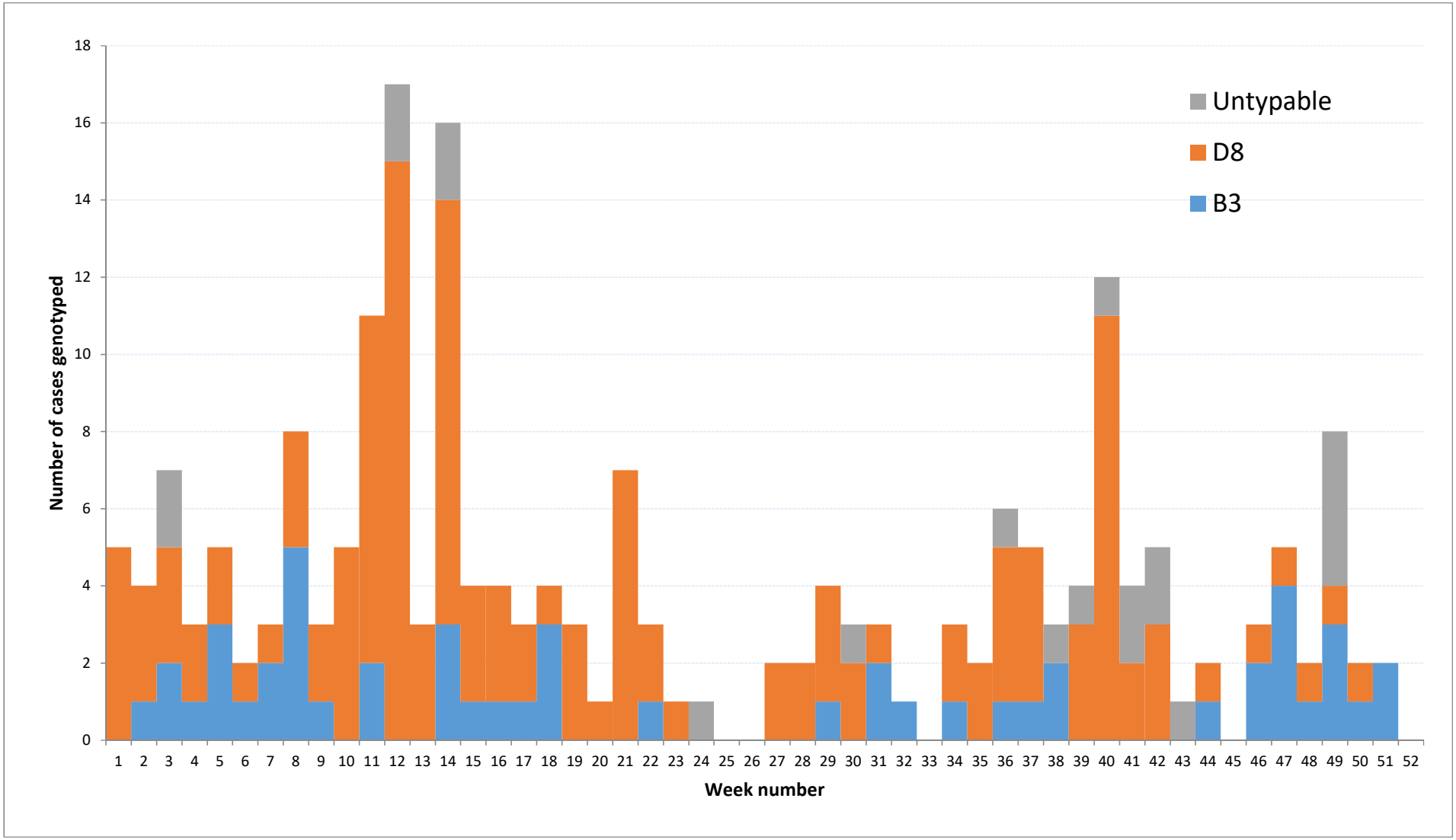
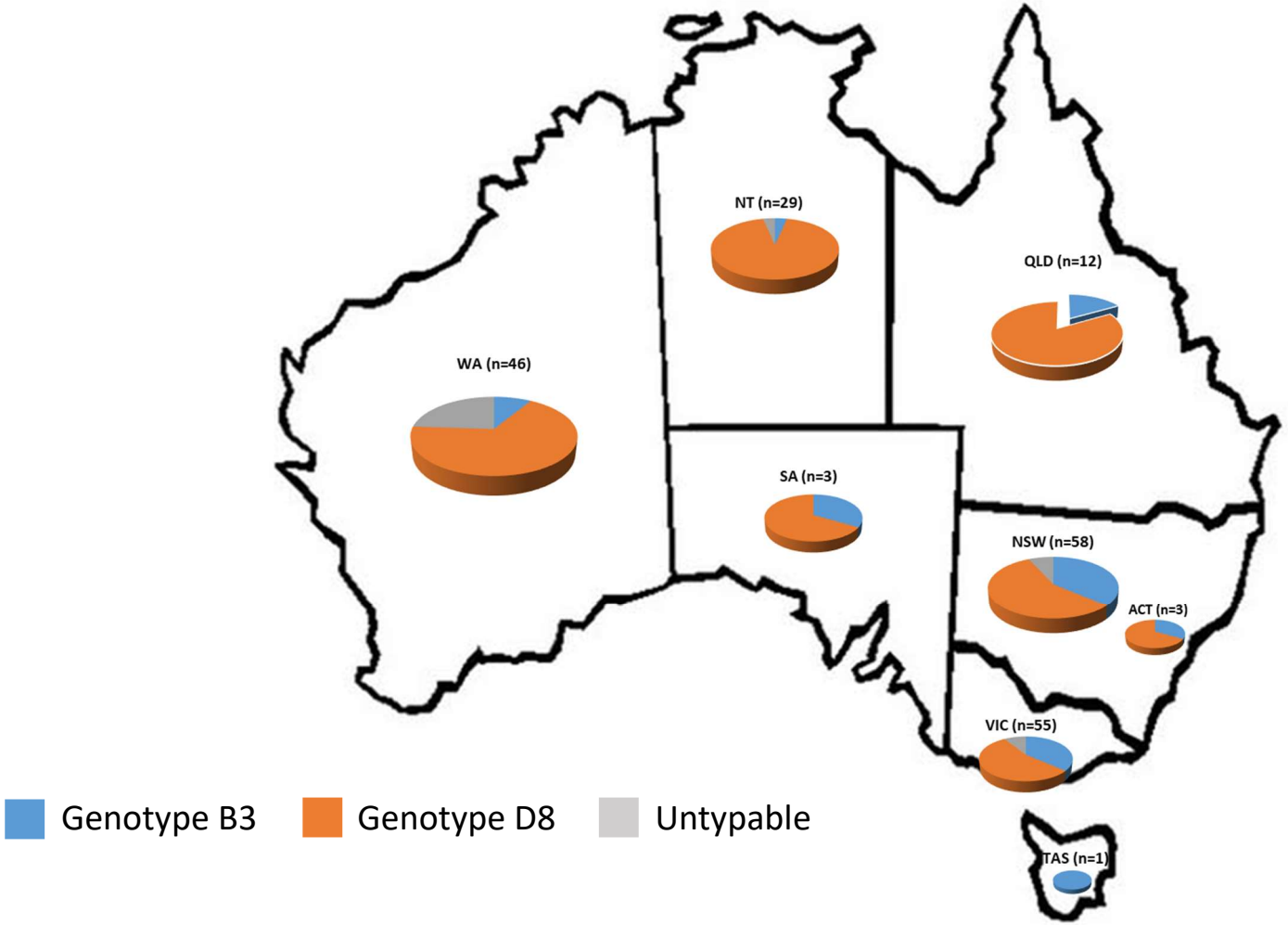
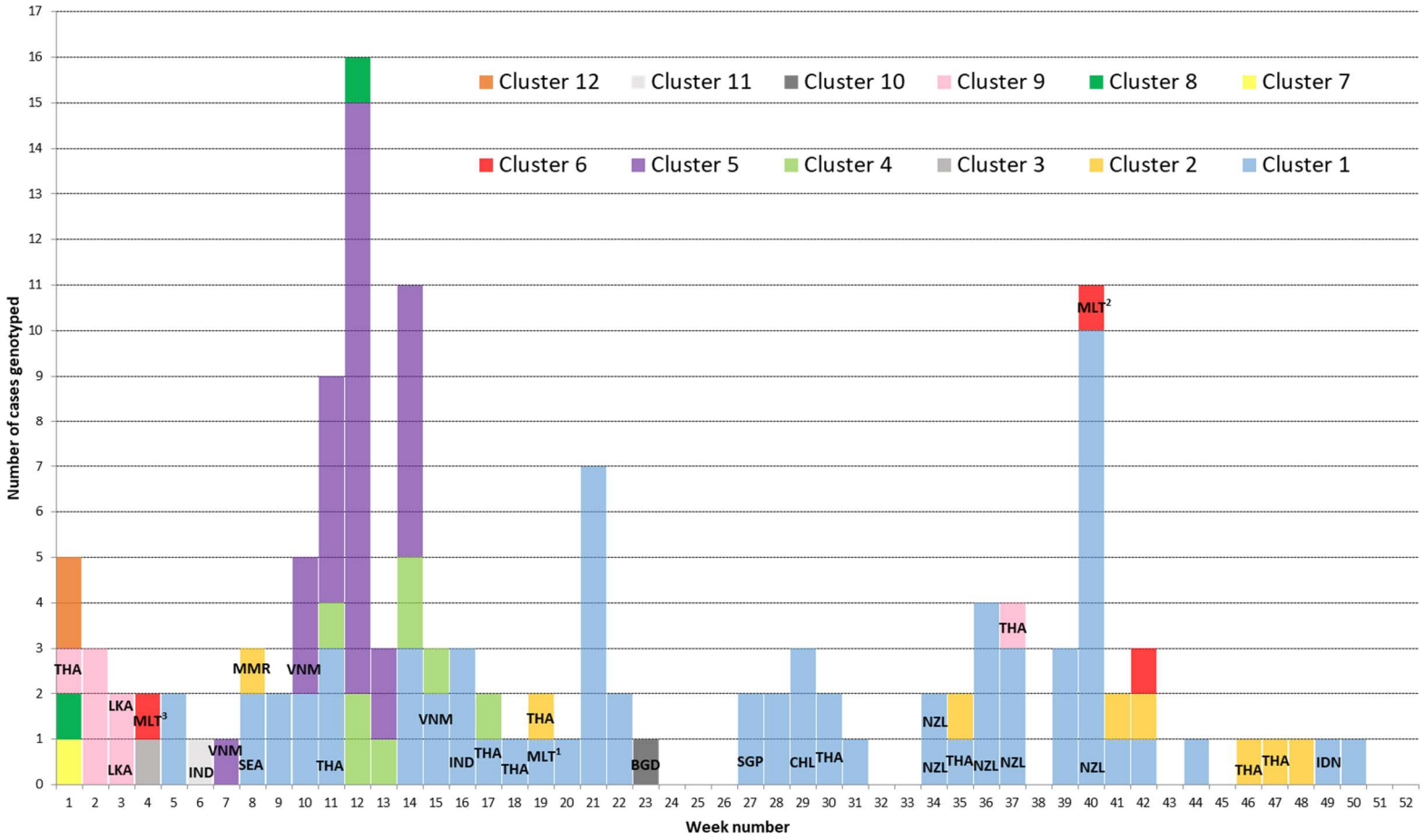


Figure 2: Geographical distribution of measles genotypes in Australia, 2019



Note: size of pie charts not proportional to the number of cases genotypes.

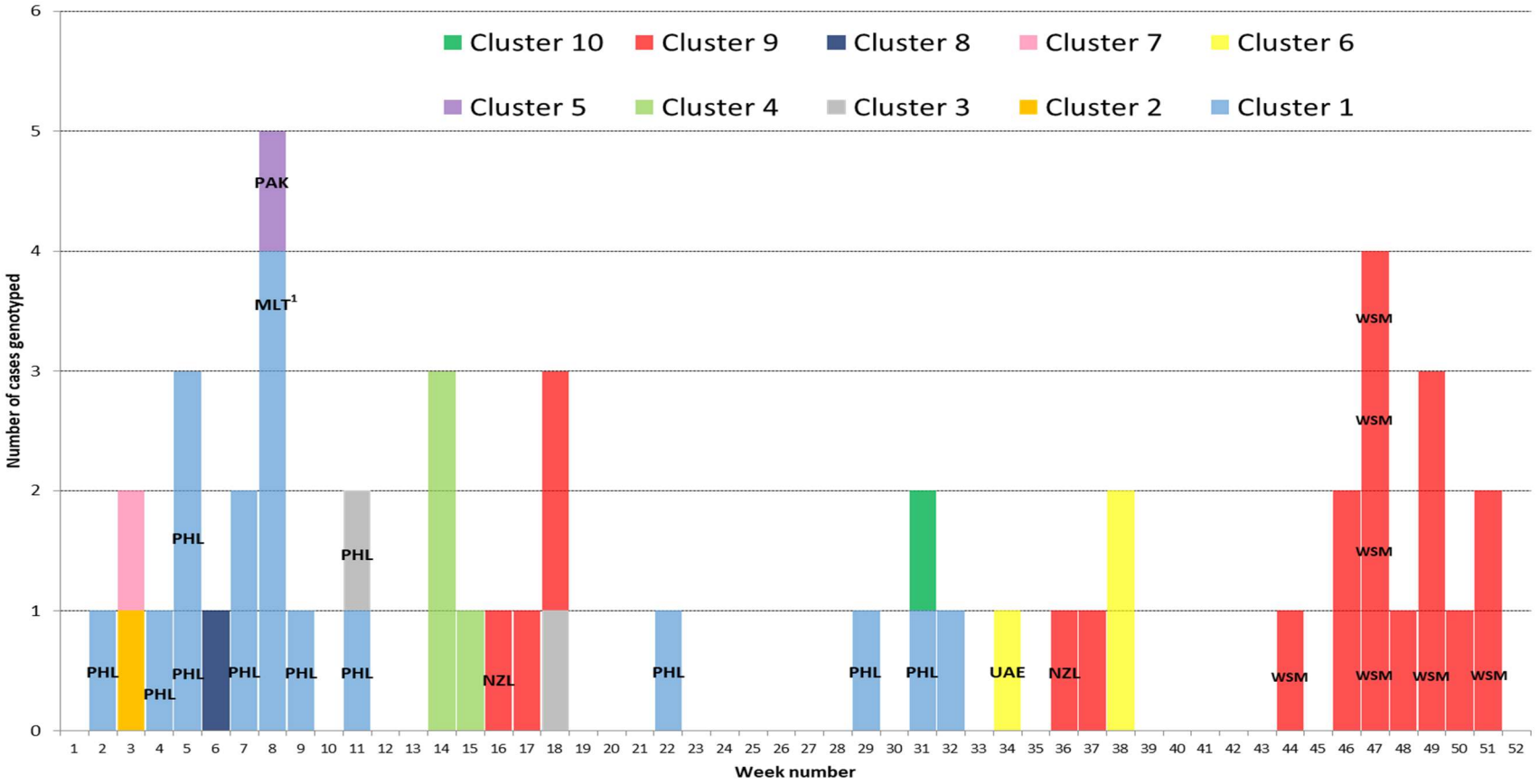
Figure 3: Distribution of measles genotype D8 genetic clusters by epi-week, January to December 2019.



Genetic clusters determined by Figure 5 phylogeny.

Country/region codes associated with imported measles cases are indicated (BGD=Bangladesh; CHL=Chile; IDN=Indonesia; IND=India; LKA=Sri Lanka; MMR=Myanmar; SEA= South East Asia; THA=Thailand; VNM=Vietnam; MLT[1]=Vietnam/Cambodia; MLT[2]=Laos/Thailand; MLT[3]=Malaysia/Singapore)

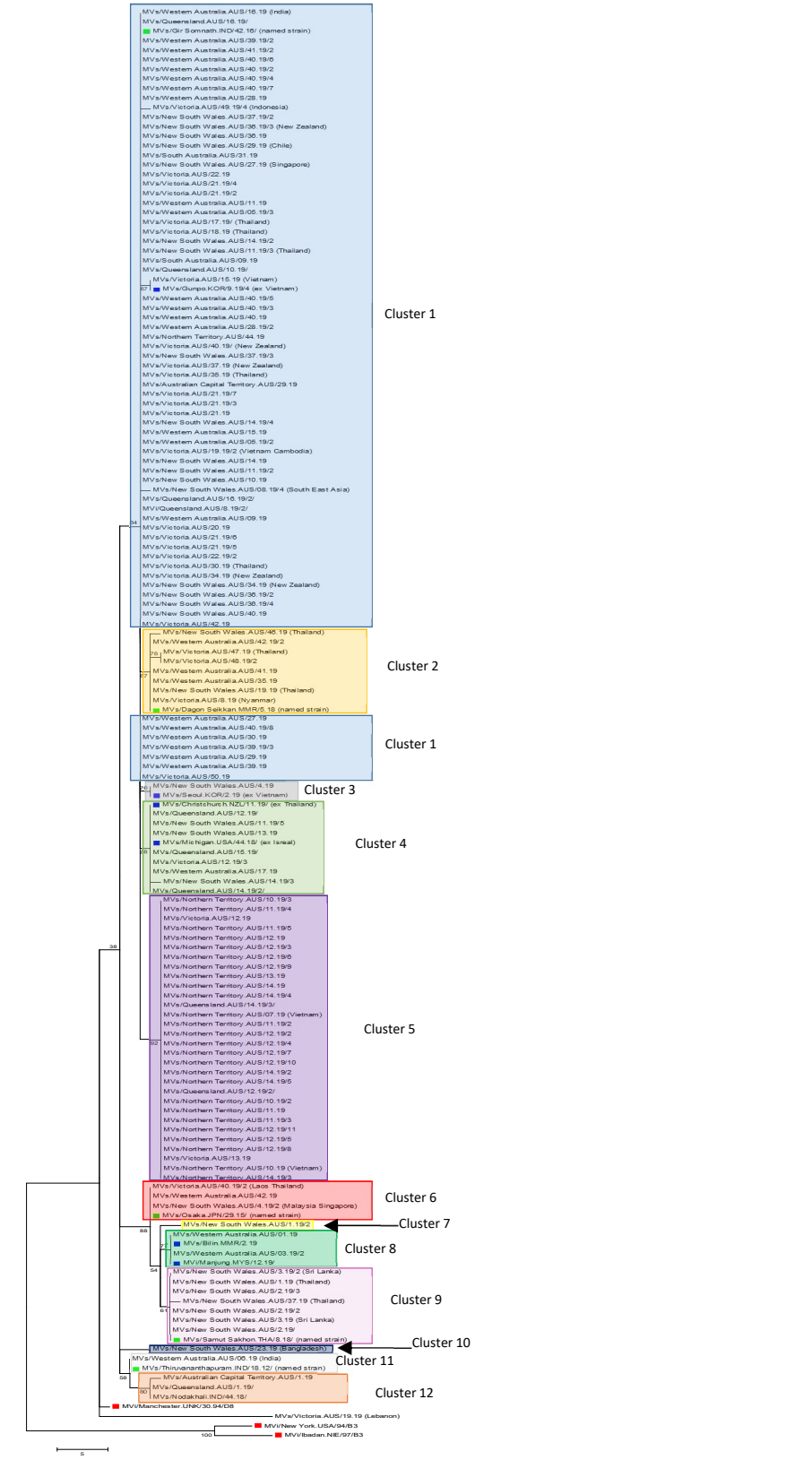
Figure 4: Distribution of measles genotype B3 genetic clusters by epi-week, January to December 2019.



Genetic clusters determined by Figure 6 phylogeny.

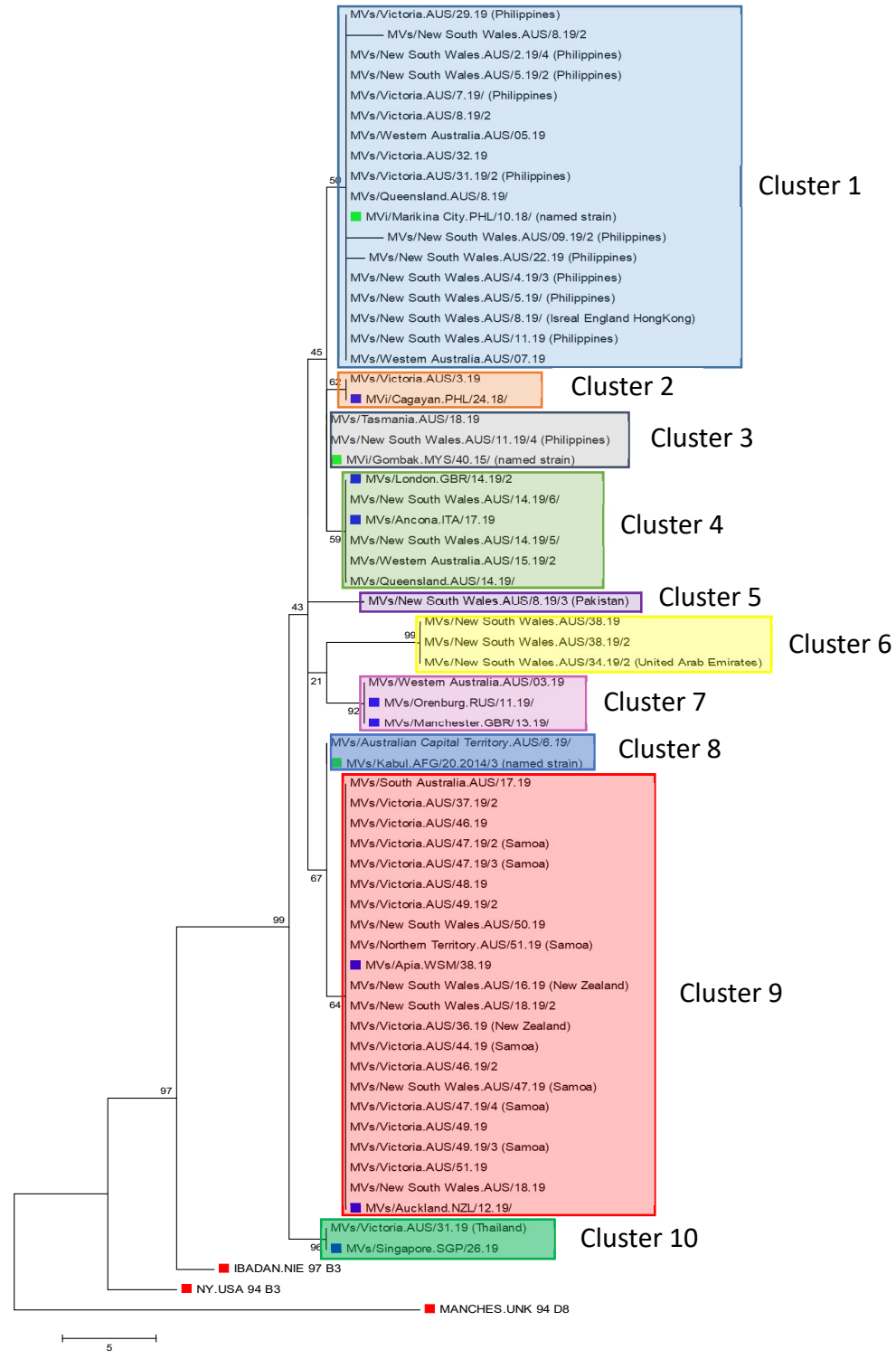
Country codes associated with imported measles cases are indicated (NZL=New Zealand; PAK=Pakistan; PHL=Philippines; UAE=United Arab Emirates; WSM=Samoa; MLT[1]=Israel/England/Hong Kong SAR, China).

Figure 5: N450 phylogenetic relationships among measles genotype D8 strains identified in Australia, 2019.



Source country of measles virus provided in parenthesis.

Figure 6: N450 phylogenetic relationships among measles genotype B3 strains identified in Australia, 2019.



WHO reference strain Strain match in MeaNS database Measles named strain

Source country of measles virus provided in parenthesis.